

ABSTRACT

RETRONS FOR GENE TARGETING

5 The invention provides methods and nucleic acid constructs that may be used to modify a nucleic acid of interest at a target locus within the genome of a host. In some aspects, the invention contemplates producing *in vivo* a gene targeting substrate (GTS), which may be comprised of both DNA and RNA components. The gene targeting substrate may comprise a gene targeting nucleotide sequence (GTNS), which is homologous to the target locus, but
10 comprises a sequence modification compared to the target locus. The gene targeting substrate may be produced by reverse transcription of a gene targeting message RNA (gtmRNA). The gene targeting message RNA may be folded for self-priming for reverse transcription by a reverse transcriptase. The gene targeting message RNA may in turn be the product of transcription of a gene targeting construct (GTC) encoding the gene targeting message RNA. The
15 gene targeting construct may for example be a DNA sequence integrated into the genome of the host, or integrated into an extrachromosomal element. Following expression of the gene targeting systems of the invention, hosts may for example be selected having genomic modifications at a target locus that correspond to the sequence modification present on the gene targeting nucleotide sequence. In some embodiments, the structure of retrons may be adapted for use in
20 the gene targeting systems of the invention.